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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,295	09/09/2002	Menachem Rubinstein	RUBINSTEIN=7	2828
1444 7590 04/05/2007 BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, NW SUITE 300 WASHINGTON, DC 20001-5303			EXAMINER CHANDRA, GYAN	
			ART UNIT 1646	PAPER NUMBER
SHORTENED STATUTORY PERIOD OF RESPONSE 3 MONTHS		MAIL DATE 04/05/2007		DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/070,295

Applicant(s)

RUBINSTEIN ET AL.

Examiner

Gyan Chandra

Art Unit

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 27 February 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5,9,11,12 and 15-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5,9,11,12 and 15-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on 2/27/2007 has been entered.

Status of Application, Amendments, And/Or Claims

The amendments of claim 9 have been made of record.

Claims 5, 9, 11-12 and 15-18 are pending.

Claims 5, 9, 11-12 and 15-18 are examined on the merit to the extent that they read on the elected invention of VEGF inhibitor – CSC.

Response to Arguments

Claim Rejections-withdrawn

Claim Rejections - 35 USC § 112, second paragraph

The rejection of claim 9 under 35 U.S.C. 112, second paragraph is withdrawn due to Applicant's amendment of claim 9.

Claim Rejections - 35 USC § 112-written description

The rejection of Claims 5, 9, 11-12 and 15-18 under 35 U.S.C. 112, first paragraph-written description is withdrawn in view of Applicants arguments and the enclosures (WO 00/47741, WO 96/05309 and US Pat No. 5,831017)

Claim Rejections-maintained

Claim Rejections - 35 USC § 112-enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 9, 11-12 and 15-18 stand rejected under 35 U.S.C. 112, first paragraph-enablement for the reasons of record on pages 5-10 of the Office Action mailed on 2/13/2006 and on pages 4-5 of the Office Action mailed on 9/28/2006.

Claims 5, 9, 11-12 and 15-18 are drawn to a method for inhibiting angiogenesis in mammals comprising administering to a subject a pharmaceutical composition comprising (i) leptin, (ii) a leptin fragment, (iii) a leptin homolog having 90% sequence identity with sequence of leptin, or (iv) a derivative of leptin or leptin homolog which has the activity of leptin, and optionally, an inhibitor of angiogenesis in a suitable dosage, (v) wherein angiogenesis inhibitor is a VEGF inhibitor, (vi) wherein the derivative said derivative has one or more chemical moieties attached to leptin, (vii) wherein said chemical moieties are water soluble polymers, and wherein said polymers are polyethylene glycol.

Applicants argue (page 7 of Response) that (i) in Example 1 of the instant specification ob -/- mouse (leptin KO mouse) was used as a model to test the anti-angiogenic effect of leptin; however, it is not that no anti- angiogenic effect

Art Unit: 1646

was observed for leptin in normal mice but simply that no experiments were conducted in normal mice. Applicants argue (page 8-12) that (ii) it is not undue experimentation to make mutations in leptin that would result in more than 10% variation in the encoded protein and that one of skill in the art, usually requiring a Ph.D. would consider this to be routine experimentation. Applicant argues that (iii) leptin induces Ang-2 mRNA expression in differentiated 3T3-F442A murine adipocytes and cites Cohen et al. (2001).

Applicants' arguments regarding the use of ob -/- mouse model have been fully considered but they are not persuasive because it is well known in the art that the patho-physiology of a KO model, in general, differs from a normal animal. For example, Sierra-Honigmann et al. teach that when they administered leptin in normal or leptin deficient fa/fa Zucker fatty rats (which is analogous to ob -/- mouse), leptin response was quite different. They teach that in normal rats, leptin caused a vigorous angiogenic response whereas leptin had no angiogenic effect in fa/fa rats (page 1685, middle column). Further, Sierra-Honigmann et al. teach that it is leptin, which is unable to induce angiogenesis in a leptin deficient rat while other angiogenic agents (e.g., VEGF) still induce angiogenesis (page 1685, middle column). Therefore, one of skill in the art would use a normal mouse, not a leptin deficient mouse, for administering leptin to see its response on angiogenesis as taught by Sierra-Honigmann et al, supra.

Applicants arguments regarding leptin induces Ang-2 gene expression in differentiated 3T3-F442A murine adipocytes are persuasive, but the method of inhibiting angiogenesis in mammals comprising administering leptin is not

Art Unit: 1646

persuasive. Further, applicants arguments regarding making and using leptin homologues (10 % variants) and the references cited in support of applicants' arguments are persuasive and being withdrawn. However, because of the lack of enablement for inhibiting angiogenesis in mammals comprising administering to a subject comprising leptin, a leptin fragment, or a leptin homolog having 90% sequence identity with sequence of leptin is maintained.

Conclusion

No claim is allowed.

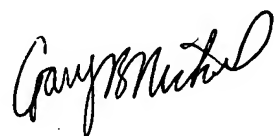
Art Unit: 1646

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gyan Chandra whose telephone number is (571) 272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gyan Chandra, Ph.D.
Art Unit 1646
22 March 2007
Fax: 571-273-2922



GARY B. NICKOL, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600